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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/806,611	03/22/2004	Mary Collins	01997.043200	2470

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EXAMINER	
WANG, CHANG YU	

ART UNIT	PAPER NUMBER
1649	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/806,611	COLLINS ET AL.	
	Examiner	Art Unit	
	Chang-Yu Wang	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 April 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-15,17-36 and 38-49* is/are pending in the application.

4a) Of the above claim(s) *20-28 and 41-49* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3-15, 17-19, 29-36 and 38-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

RESPONSE TO AMENDMENT

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4/10/08 has been entered.

Status of Application/Amendments/claims

2. Applicant's amendment filed 2/11/08 is acknowledged. Claims 2, 16, and 37 are cancelled. Claims 1, 17, 29, 34 and 35 are amended. Claims 1, 3-15, 17-36, and 38-49 are pending in this application. Claims 20-28 and 41-49 are withdrawn without traverse (the response filed 8/23/06) from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

3. Claims 1, 3-15, 17-19, 29-36 and 38-40 are under examination with respect to IFN-1α/β in this office action.

4. Any objection or rejection of record, which is not expressly repeated in this action has been overcome by Applicant's response.

5. Applicant's arguments filed on 2/11/08 have been fully considered but they are not deemed to be persuasive for the reasons set forth below.

Claim Rejections/Objections Maintained

In view of the amendment filed on 2/11/08, the following rejections are maintained.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3-15, 17-19, 29-36 and 38-40 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for increasing production of IL-10 and decreasing INF-γ IL-1α, IL-2, IL-6, IL-18 and increasing T cell proliferation in an EAE animal model by administration of the IL-21 polypeptide of SEQ ID NO:2 to decrease the severity of symptoms that are regulated by inappropriate cytokine production, does not reasonably provide enablement for treating, preventing or ameliorating multiple sclerosis associated with an IL-10 deficiency, increased IFN-γ, increased IL-1a, increased IL-2, increased IL-6 or increased IL-18 or other disorders associated with an IL-10 deficiency by administering to a subject any unknown agonist of IL-21/IL-21R as broadly claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The rejection is maintained for the reasons made of record in the office actions mailed 8/10/07 & 3/20/08, and as follows.

At p. 13-15 of the response filed 2/11/08, Applicant argues that the claimed method is enabling because making and determining an agonistic anti-IL-21R antibody

are routine. At p. 16-17 of the response, Applicant argues that amended claims are enabled because the specification provides support for treating or ameliorating MS or a symptome thereof based on the EAE mouse model. Applicant's arguments have been fully considered but they are not persuasive.

In contrast, the claims are not limited to use of agonistic IL-21R antibodies. The claims encompass use of a genus of IL-21 polypeptides and use of a genus of agonistic anti-IL-21R antibodies. However, as previously made of record, the specification fails to provide sufficient guidance as to how to make the claimed genus of IL-21 polypeptides. In addition, although screening for an agonistic anti-IL-21R antibody that is generated from a defined sequence is routine, the claims are not limited to an antibody against a specific defined sequence of IL-21R because IL-21R encompasses structurally undefined variants. Further, the specification fails to teach what specific structures and sequences are requried for generating agonistic anti-IL-21R antibodies since the IL-21R polypeptide is not limited to a single amino acid sequence but also encompasses variants and a genus of polypeptides that are not structurally and functionally defined by the specification. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without such guidance, the changes which can be made and still maintain activity is unpredictable and the experimentation left to those skilled in the art is extensive and undue. See Ex parte Forman, 230 USPQ 546 (Bd. Pat. App. & Int. 1986). Thus, the skilled artisan cannot readily make and use the claimed invention as currently claimed without further undue experimentation.

At p. 16-17 of the response filed 2/11/08, Applicant argues that amended claims are enabled because instant claims have been amended to recite treating and ameliorating MS by an agonist of IL-21/IL-21 receptor and the specification provides such support in the examples. Applicant's arguments have been fully considered but they are not persuasive.

In contrast, as previously made of record, the amended claims still recite "treating" which encompasses curing as defined by the specification. However, neither the specification nor the prior art provides support to cure MS or its related symptoms by any agonist of IL-21/IL-21R. Thus, the instant invention is not enabled commensurate in scope with the claims or with the specification. Note that

"The 'predictability or lack thereof' in the art refers to the ability of one skilled in the art to extrapolate the disclosed or known results to the claimed invention. If one skilled in the art can readily anticipate the effect of a change within the subject matter to which the claimed invention pertains, then there is predictability in the art. On the other hand, if one skilled in the art cannot readily anticipate the effect of a change within the subject matter to which that claimed invention pertains, then there is lack of predictability in the art. Accordingly, what is known in the art provides evidence as to the question of predictability. In particular, the court in In re Marzocchi, 439 F.2d 220, 223-24, 169 USPQ 367, 369-70 (CCPA 1971)" See MPEP § 2164.03.

In addition, a patent is granted for a completed invention, not the general suggestion of an idea and how that idea might be developed into the claimed invention. In the decision of *Genentec, Inc, v. Novo Nordisk*, 42 USPQ 2d 100,(CAFC 1997), the court held that:

"[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable" and that "[t]ossing out the mere germ of an idea does not constitute enabling disclosure". The court further stated that "when there is no disclosure of any specific starting material or of any of the conditions under which a process is to be carried out, undue experimentation is required; there is a failure to meet the enablement requirements that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art", "[i]t is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement".

7. Claims 1, 29-30, 32-36 and 38-40 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The rejection is maintained for the reasons made of record in the office actions mailed 8/10/07 & 3/20/08, and as follows.

At p. 18 of the response filed 2/11/08, Applicant argues that the claims are limited to an IL-21 polypeptide with an example of SEQ ID NO:2, agonistic anti-IL-21R antibody or antigen-binding fragment of the agonistic anti-IL-21R antibody. Applicant argues that the specification has provide sufficient guidance as to screen for all agonistic anti-IL-21R antibodies. Applicant's arguments have been fully considered but they are not persuasive.

In response, as previously made of record, the recitation of "IL-21 polypeptide" in instant claims is not limited to the amino acid sequence of SEQ ID NO:2 or 95% identity to SEQ ID NO:2. The specification defines "an IL-21 polypeptide" as including fragments of IL-21 and homologues with 30-95% identity to SEQ ID NO:2 on p. 18-20. However, the specification fails to teach what common structures and amino acid sequences are requried for the claimed genus of IL-21 polypeptides to be used in the claimed method. In addition, the specification fails to limit to IL-21R polypeptide and what sequence is required to generate an agonistic anti-IL-21R antibody. Thus,

Applicant was not reasonably in possession of the "claimed genus of IL-21 polypeptides and the claimed genus of anti-IL-21R antibody and its antigen-binding fragments" that can be used in the claimed method. Note that

> A definition by function alone "does not suffice" to sufficiently describe a coding sequence "because it is only an indication of what the gene does, rather than what it is." *Eli Lilly*, 119 F.3 at 1568, 43 USPQ2d at 1406. See also *Fiers*, 984 F.2d at 1169-71, 25 USPQ2d at 1605-06 (discussing *Amgen Inc. v.Chugai Pharmaceutical Co.*, 927 F.2d 1200, 18 USPQ2d 1016 (Fed. Cir. 1991)). An adequate written description of a chemical invention also requires a precise definition, such as by structure, formula, chemical name, or physical properties, and not merely a wish or plan for obtaining the chemical invention claimed. See, e.g., *Univ. of Rochester v. G.D. Searle &Co.*, 358 F.3d 916, 927, 69 USPQ2d 1886, 1894-95 (Fed. Cir. 2004).

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 17-19 and 34-40 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The rejection is maintained for the reasons made of record in the office actions mailed 8/10/07 & 3/20/08, and as follows.

At p. 17 &19 of the response, Applicant argues that the rejection is moot because the specification clearly describes the term "IL-10 parameter" at [0014] & [0028] comprising quantitative and qualtative information. Applicant's arguments have been fully considered but they are not persuasive.

In contrast, the specification only describes examples to assay or evaluate IL-10 activity but fails to limit what specific parameter and activity of IL-10 are and thus would be within the scope of the claims. The disclosure fails to set forth the metes and bounds

of what is encompassed within the definition of "an IL-10 parameter" and thus the claims are indefinite.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1,3-4, 9-12, 14 and 29-34 stand rejected under 35 U.S.C. 102 (e) as being anticipated by Novak et al. (US Patent No. 6605272, issued Aug 12, 2003, priority date Mar 9, 1999, as cited in IDS submitted May 23,2006). The rejection is maintained for the reasons made of record in the office actions mailed 8/10/07 & 3/20/08, and as follows.

At p.20-21 of the response filed 2/11/08, Applicant argues that the '272 patent does not anticipate the claimed method and does not provide an enabling disclosure for such method because the '272 patent does not teach a method of treating or ameliorting MS asscoiated with an IL-10 deficiency or increased IFN-γ in patient. Applicant further cites *Verdegaal Bros. v. Union Oil Co.of California* and *In re Hoeksema* in support of the arguments. Applicant's arguments have been fully considered but they are not persuasive.

In contrast, the examiner asserts that the '272 patent is enabling for the instant claims because the '272 patent discloses the claimed method and a prior art of an issued US patent is a reference containing an "enabling disclosure" that the public was in possession of the claimed invention before the date of invention. In *In re Donhue*, the court held that

"A reference contains an "enabling disclosure" if the public was in possession of the claimed invention before the date of invention. "Such possession is effected if one of ordinary skill in the art could have combined the publication's description of the invention with his [or her] own knowledge to make the claimed invention." In re Donohue, 766 F.2d 531, 226 USPQ 619 (Fed. Cir. 1985)." See MPEP 2121.01 [R3].

The '272 patent does teach the claimed method of ameliorating MS symptoms by IL-21 polypeptides because the '272 patent teaches the same active step (i.e.administration of IL-21 as claimed) and the same material (i.e. IL-21 polypeptide), and the same patient population (i.e. MS). The '272 patent teaches a therapeutic use of IL-21 (ZALPHA11 ligand) in several immunological disorders including multiple sclerosis as recited in instant claims 1, 3-4, 9-12 and 29-34 (see col. 42, lines 9-31; col.192-198, claims 1-21, in particular). The '272 patent teaches that IL-21 enhances proliferation of CD4+ T cells, CD8+ cytotoxicity T cells and Natural killer cells and also teaches that IL-21 enhances regulating production of cytokines such as increasing IL-10 or decreasing IFN-γ to treat immunological disorders mediated by cellular immunity as recited in instant claims 1, 29, 34 (see col.99-102, examples 41-42). The limitation of ameliorating a symptom of MS or MS associated with an IL-10 deficiency or increased IFN-γ would be an inherent result of administration of IL-21 because IL-21 enhanes secretion of IL-10 and decreases IFN-γ and thereby reverses the condition of IL-10 deficiency and

increased IFN-γ in MS. Thus, the '272 patent anticipates the claimed method as recited in instant claims.

At p. 22 of the response, Applicant argues that the examiner has not satisfied the required burden to show the claimed method is inherently disclosed in the '272 patent and cites MPEP 2112 in support of the arguments. Applicant argues that '272 patent does not inherently disclose the claimed method because IL-21 may affect the proliferation of immune cells but does not mean the '272 patent teaches IL-21 mediated regulation of cytokines, in particular IL-10 as recited in instant claims. Applicant's arguments have been fully considered but they are not persuasive.

In contrast, the examiner has made a prima fascia case to establish that the '272 patent discloses the claimed method on p. 11 of the office action mailed 8/10/07. The examiner asserts that Applicant is incorrect with regard to Applicant's argument that the '272 patent does not teach regulation of T cells and cytokines by IL-21. The examiner asserts that the '272 patent does teach that IL-21 enhances proliferation of $CD4^+$ T cells, $CD8^+$ cytotoxicity T cells and Natural killer cells and also enhances regulating production of cytokines such as increasing IL-10 decreasing IFN-γ to treat immunological disorders mediated by cellular immunity as in instant claims 1, 29, 34 (see col.99-102, examples 41-42). The limitation of "ameliorating a symptom of MS or MS associated with an IL-10 deficiency or increased IFN-γ" would be an inherent result of regulating immune responses of T cell proliferation and production of cytokines by administration of IL-21 (i.e. an agonist of the IL-21 receptor by definition) as recited in

instant claims 1-4, 9-12, 29-31 and 34 because the '272 patent teaches the same active steps of administration of IL-21, the same material (i.e. IL-21) and the same patient population as claimed. As previously made of record, the limitations of "enhancing secretion of IL-10 and decreasing IFN-γ by IL-21" are inherent results as evidenced by Wurster et al.. In addition, note that no other active steps are recited in the claimed method as in instant claims 1,3-4, 9-12, 14 and 29-34. The limitation of ameliorating MS associated with an IL-10 deficiency or increased IFN-g would be an inherent result of administration of IL-21 because IL-21 enhances secretion of IL-10 and decreases IFN-γ and thereby reverses the condition of IL-10 deficiency and increased IFN-γ in MS, which is the immune responses of T cell proliferation and production of cytokines regulated by IL-21 as evidenced by Wurster et al.. Note that

"Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established. In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). 'When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not.' In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Therefore, the prima facie case can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product. In re Best, 562 F.2d at 1255, 195 USPQ at 433." See MPEP § 2112.01 [R-3].

"The discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." Atlas Powder Co. v. Ireco Inc., 190 F.3d 1342,1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Thus the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. In re Best, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977). " See MPEP § 2112.01 [R-3].

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1,3-15,17-19, and 29-34 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Novak et al. (US Patent No. 6605272, issued Aug 12, 2003, priority date Mar 9, 1999, as cited in IDS submitted May 23,2006) in view of Carter et al. (US20030108549A, published Jun 12, 2003, priority date Oct 4, 2001) and Kawai et al. (Cell Immunol. 1996. 171:262-8). The rejection is maintained for the reasons made of record in the office actions mailed 8/10/07 & 3/20/08, and as follows.

At p. 23 of the response filed 2/11/08, Applicant argues that the '272 patent does not teach modulation of IL-10 or IFN-r by IL-21 or a method of treating or ameliorating MS by IL-21, thus the combination with the '549 publication and Kawai et al does not render the claimed method obvious. Applicant's arguments have been fully considered but they are not persuasive.

In contrast, the '272 patent does teach the limitation of the claims 1, 3-4, 9-12, 14 and 29-34 as set forth above at paragraph 9 and in the office action mailed 8/10/07. Although the '272 patent does not teach an agonistic anti-IL-21 antibody and an anti-

inflammatory agent, the '549 publication teaches an agonistic anti-IL-21R antibody as recited in instant claims 1 and 5-6 (see p. 3 [0023], p.5 [0041]) and use of a combination of anti-inflammatory agent including IFN-1α/β and an IL-21/IL21R agonist to treat T cell-mediated diseases such as tumor as it relates to claims 7-8 (see p.3 [0024], p.5 [0039], [0040], [0208]). In addition, the '549 publication also teaches that an IL-21/IL21R agonist enhances T cell proliferation and cytokine regulation, which relates to ameliorating a symptom of MS associated with cytokines (IL-10 and IFN-γ). Although the '272 patent and the'549 publication do not teach injection of IL-21 agonists into the CNS as recited in instant claims 13-15, Kawai et al. teach administering monoclonal antibodies that are against LFA-1 and ICAM-1 in an EAE rat model (a MS animal model) by intracerebroventricular and intrathecal administration routes. Thus, the claimed method is obvious over the applied references.

11. Claims 1,3-15,17-19,29-36 and 38-40 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Novak et al. (US Patent No. 6605272, issued Aug 12, 2003, priority date Mar 9, 1999, as cited in IDS submitted May 23,2006), Carter et al. (US20030108549A, published Jun 12, 2003, priority date Oct 4, 2001) and Kawai et al. (Cell Immunol. 1996. 171:262-8) as applied in claims 1-15, 29-34 above and further in view of Beebe et al. (Cytokine & Growth Factor Rev. 2002. 13: 403-12 as in IDS submitted on 05/23/06). The rejection is maintained for the reasons made of record in the office actions mailed 8/10/07 & 3/20/08, and as follows.

At p. 24 of the response filed 2/11/08, Applicant argues that the '272 patent does not teach the claimed method and a skilled artisan would not be motivated to combine the teachings of the '549 publication and Kawai to reach the claimed invention. Applicant argues that although Beebe teaches that the level of IL-10 is low in MS, it does not provide a nexus between IL-21 and treatment of MS to have a motivation and expectation of success in treating MS associated with IL-10 deficiency by adminstration of an agonist of IL-21/IL-21R. Applicant's arguments have been fully considered but they are not persuasive.

In contrast, the '272 patent does teach the limitation of the claims 1, 3-15,17-19, and 29-34 as set forth above.The teachings of Beebe provide a motivation and expectation of success in evaluating the level of IL-10 in MS patients before and after treatment because Beebe teaches that the level of IL-10 is low in MS. Thus, it would have been obvious to a skilled artisan to ameliorate a symptom of MS regulated by inappropriate production of IL-10 and IFN-r by incorporating the teachings of Beebe et al. to measure/monitor the levels of IL-10 in MS patients while practicing the claimed method of the '272 patent, and '549 publication and Kawai et al. because a low level of IL-10 is found in MS and EAE, and the level of IL-10 increases after a successful treatment of MS patients.

Conclusion

12. NO CLAIM IS ALLOWED.

13. All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

14. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Papers relating to this application may be submitted to Technology Center 1600, Group 1649 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chang-Yu Wang whose telephone number is (571) 272-

4521. The examiner can normally be reached on Monday-Thursday from 8:30 AM to 6:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker, can be reached at (571) 272-0911.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/CYW/
Chang-Yu Wang, Ph.D.
June 16, 2008

/Jeffrey Stucker/
Supervisory Patent Examiner, Art Unit 1649